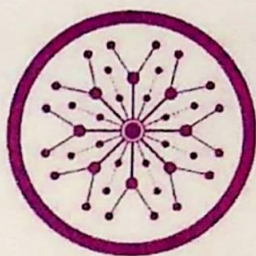


**The Impact of Ketamine on Postoperative Nausea, Vomiting and
Cognitive Dysfunction in Diabetic Patients Undergoing Laparoscopic
Cholecystectomy**



SUPERIOR UNIVERSITY

Thesis Submitted to

The Superior University Lahore

In Partial Fulfillment of the

Requirement for the Degree of

MS Allied Health Sciences

By

AMNA SALEEM

SU91-MSAHW-S23-025

Session 2023-2025

Faculty of Allied Health Sciences

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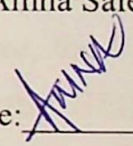
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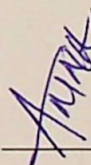
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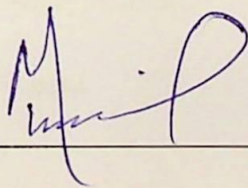


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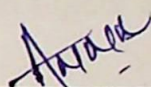
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No part of this thesis has been submitted anywhere else for any other degree. This thesis is submitted to the Faculty of Allied Health Sciences, The Superior University, Lahore in partial fulfillment of the requirements for the degree of Master of Sciences in the field of “**Allied Health Sciences**” in Faculty of Allied Health Sciences at The Superior University, Lahore.

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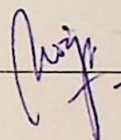
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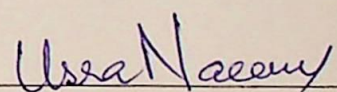
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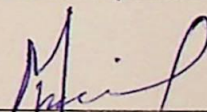
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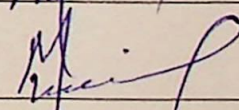
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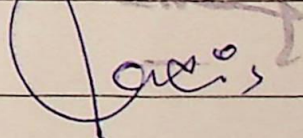
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DEDICATION

This thesis is dedicated to my parents, whose unwavering support, unconditional love, and constant encouragement have been the foundation of my journey. Your sacrifices and belief in me have been my greatest strength.

To my family, thank you for being my pillars of support, for celebrating my successes, and for standing by me in times of struggle. Your presence has made this achievement all the more meaningful.

I am deeply grateful to each of you for inspiring me to reach higher and pursue my dreams.

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Amna Saleem

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LIST OF ABBREVIATIONS

PONV	Postoperative Nausea and Vomiting
CD	Cognitive Dysfunction
LC	Laparoscopic Cholecystectomy
DM	Diabetes Mellitus
RCT	Randomized Controlled Trial
ASA	American Society of Anesthesiologists
HR	Heart Rate
BP	Blood Pressure
CI	Confidence Interval
IV	Intravenous
SPSS	Statistical Package for the Social Sciences
SD	Standard Deviation
VAS	Visual Analog Scale
GCS	Glasgow Coma Scale
CNS	Central Nervous System
PACU	Post-Anesthesia Care Unit
EEG	Electroencephalogram
BMI	Body Mass Index
NMDA	N-Methyl-D-Aspartate (receptor, target of ketamine)
ANOVA	Analysis of Variance

Background: This study sought to discover factors impacting the prevalence of postoperative nausea and vomiting (PONV) and postoperative delirium (PONV), which are common sequelae in diabetic patients after elective laparoscopic cholecystectomy.

Methods: The cross-sectional study included 163 diabetic patients scheduled for elective laparoscopic cholecystectomy. Patients were assessed for delirium at 2, 4, 6, and 8 hours post-op using the RASS and the CAM-ICU, two instruments designed for use in the intensive care unit. The characteristics that were studied were patients' body mass index (BMI), hemoglobin A1c (HbA1c) levels, the duration of the operation, fasting blood sugar, and evaluations of liver and kidney function. Postoperative nausea and vomiting were also noted of patients.

Results: At 2 hours after surgery, the rate of delirium was 18.4% (n=30) and at 4 hours, it dropped to 15.3% (n=25) and at 6 hours, it dropped to 12.3% (n=20). Finally, at 8 hours, it dropped to 9.2% (n=15). No statistically significant correlation between delirium and age, gender, profession, or length of diabetes duration was found ($p > 0.05$). Delirium was more common in overweight and obese patients, while the correlation between body mass index and delirium was not statistically significant ($p = 0.04$). Additionally, delirium rates were lower in patients whose hemoglobin A1c levels were below 6.5% ($p = 0.03$) and in patients whose operations lasted less than an hour ($p = 0.02$). Postoperative nausea and vomiting (PONV) were more common in patients with type II diabetes ($p = 0.005$), hemoglobin A1c levels higher than 7.5% ($p = 0.04$), and procedures lasting one to two hours ($p = 0.03$). Further, elevated fasting blood sugar levels ($p = 0.02$) above 180 mg/dL and abnormal liver function tests ($p = 0.04$) both substantially predicted PONV.

Conclusion: The study discovered that delirium became much less common with time; at 2 hours after surgery, the prevalence was 18.4%; at 8 hours, it had dropped to 9.2%. Potential risk factors for postoperative delirium include obesity, increased HbA1c levels, and a lengthy duration of the operation.

Keyword: Ketamine, Postoperative nausea, Vomiting, Cognitive dysfunction.

CHAPTER 1

INTRODUCTION

1.1 Post cognitive dysfunction

1.1 Delirium

Medical specialists are perplexed by the debilitating and economically significant complication known as post-operative delirium, which impacts patients after cardiac surgery. A multitude of scientific advancements has enhanced physical outcomes for patients and enabled more lenient criteria for cardiac surgical eligibility, especially regarding age and co-morbidities. About 30% of patients following cardiopulmonary bypass surgery experience postoperative delirium, a condition that significantly impacts their health, well-being, and prognosis, possibly as a result of the procedure. The delivering analgesics and sedatives to patients in the recovery phase following cardiac surgery is crucial to ensure "best practices," since mounting evidence suggests that these interventions may correlate with the onset of delirium.

Researchers examining delirium after cardiac surgery have discovered multiple pre-operative, intra-operative, and post-operative risk factors linked to central nervous system dysfunctions. Despite progress in intraoperative surgical methods and the identification of preoperative risk factors, the occurrence of postoperative delirium has remained constant throughout the past 30 years. Despite numerous conclusions, the list of risk factors continues to grow, and this harmful surgical response continues to negatively impact patients' lives, potentially continuing for months after recovery. Despite the prolonged ICU and hospital stays, heightened morbidity and mortality, and possible long-term cognitive deficits associated with delirium in patients, the postoperative phase following heart surgery has surprisingly garnered limited study attention. Research suggests that benzodiazepines such as Midazolam and opiates like morphine (and its derivatives) may increase memory decline and concentration impairments in the elderly, as well as heighten disorientation and delirium (4–6).

1.2 Post-operative nausea and vomiting PONV

Among the most common postoperative consequences, postoperative nausea and vomiting (PONV) persists. It causes stress for patients, increases the likelihood of further negative outcomes like readmission, and costs money for the healthcare provider. Assessing risks, implementing multimodal risk mitigation strategies, implementing preventative treatments, and providing urgent rescue treatment are all part of PONV care (7).

One common side effect of surgery and anesthesia is postoperative nausea and vomiting, or PONV (8). PONV is associated with patient discomfort and dissatisfaction with postoperative care; nonetheless, it is rarely fatal. Managing postoperative pain is less important to patients than preventing postoperative nausea and vomiting (PONV). Delays in leaving the recovery area and extended hospital stays are additional outcomes associated with PONV (9). Postoperative nausea and vomiting (PONV) are associated with a variety of complications, including wound dehiscence, dehydration, electrolyte imbalance, nutritional interference, and, on a rarer occasion, esophageal rupture (Boerhaave Syndrome) or aspiration pneumonitis. Postoperative nausea and vomiting (PONV) are associated with general anesthesia using volatile anaesthetics, with an average incidence of 20% to 30% [3]. PONV is a multi-faceted problem that includes issues related to anesthesia, surgery, and the patient themselves (10-12). Postoperative nausea and vomiting can be effectively prevented using a variety of treatments and drugs. Recently, low-dose ketamine was found to be one of the helpful drugs (13–15).

1.3 Laparoscopic cholecystectomy as a common procedure in diabetic patients

A diseased gallbladder can be removed with minimally invasive surgery using laparoscopic cholecystectomy. Regular cholecystectomies have been performed with this technique since the early 1990s, effectively replacing the open method. The following conditions can be treated by laparoscopic cholecystectomy: acute and chronic cholecystitis, biliary dyskinesia, acalculous cholecystitis, gallstone pancreatitis, gallbladder tumors or polyps, and symptomatic cholelithiasis. For an

open cholecystectomy, the indications are the same. The majority of gallbladder cancer cases are best treated with an open cholecystectomy (16,17).

Worldwide, the number of people living with diabetes is steadily increasing, with 422 million people diagnosed as of today, up from 108 million in 1980, according to the World Health Organization. Early detection and better outcomes in diabetic individuals with biliary issues are being encouraged by the increased awareness of DM due to its increasing incidence (18). The chance of gallstone formation is higher in people with diabetes, making surgical operations more dangerous for them than for nondiabetic patients. Gallstones can form for a variety of diabetic reasons, such as diabetes caused by obesity, insulin resistance, high triglyceride levels, or autonomic neuropathy. Another common ailment that goes hand in hand with the increasing prevalence of obesity is gallstone disease (GSD). Diabetic patients are more likely to have laparoscopic cholecystectomy, the gold standard procedure for symptomatic gallstone disease (GSD), than nondiabetic patients. Because high blood sugar levels weaken the immune system and impede the body's natural healing mechanisms, people with diabetes are at increased risk of infection. There are no known negative side effects of cholecystectomy, and the procedure is generally considered safe. Recent research has linked cholecystectomy to an increased risk of metabolic syndrome (MetS), with complications being much more common in diabetics compared to nondiabetics (19,20). People with diabetes are more likely to have cholecystectomy than those without the disease.

Emergency cholecystectomy, intraoperative problems, switching from laparoscopic to open cholecystectomy, and worse results compared to non-diabetics are all linked to diabetes. There has been much discussion over the past decade over when to do a cholecystectomy in cases of acute cholecystitis, with recent trends preferring laparoscopic cholecystectomy as an early intervention. So far, researchers have failed to investigate whether or not time affects outcomes in people with diabetes. Surgery for gallstone diseases, including acute and chronic cholecystitis, is associated with diabetes in 9–45% of patients. This case report details the effective management of a double gallbladder with acute cholecystitis with laparoscopic cholecystectomy (21,22).

1.4 Impact of ketamine on quality of recovery after laparoscopic surgery

Ketamine gives its analgesic effects because it is both an agonist of μ opioid receptors and a strong antagonist of NMDA (N-methyl-D-aspartate) receptors. It might be used as an induction agent or as part of a multimodal pain management program to lessen the need for opioids after surgery. As of late, ketamine has been green-lit for use in treating depression. According to recent research, a small amount of ketamine (<1 mg/kg) added to multimodal analgesia regimens is associated with fewer side effects and reduces the need for opioids after surgery as well as the negative effects of opioids, such as nausea and vomiting (23,24). However, the patient's perspective of the quality of their recovery may be impacted by the adverse effects of ketamine, which include visual and auditory hallucinations, depersonalization, and changes in physical experience, even at moderate dosages. The majority of studies employ the 40-item Quality of Recovery (QoR-40) Questionnaire, although there is a lack of research that examines how intraoperative ketamine administration affects recovery quality.

1.4.1 Clinical significance of postoperative complications such as nausea, vomiting (PONV), and cognitive dysfunction (POCD).

The main indicators of a high-quality health system are the efficiency of healthcare administration, the improvement of patient happiness, and the attainment of desired outcomes. Postoperative nausea and vomiting (PONV) and perioperative discomfort are two of the many documented postoperative complications ranging in severity. Symptoms of postoperative nausea and vomiting (PONV) typically manifest in the first twenty-four hours following surgery. In the first several hours after surgery, it is a common source of pain and discomfort for patients. Effective prevention of this outcome greatly improves patients' pleasure and speeds up their return to normal activities, which is sometimes extremely undesirable according to patients (25,26).

The time of patient discharge from the recovery room is affected by PONV, which is associated with longer hospital stays. As a result, ward overcrowding is worsened and healthcare expenditures rise overall. Even though PONV usually resolves on its own and seldom causes death, it does increase the risk of dehydration, abnormalities in

blood electrolytes, pneumonia due to aspiration, and, in the worst-case scenario, esophageal rupture.

1.5 Challenges in diabetic patients

Variegated physiological complications, including altered pain perception, metabolic stress, and prolonged recovery, experienced by diabetic individuals.

Situations like unemployment or unfavorable socioeconomic conditions are examples of chronic stresses that people experience for weeks or even years at a time (27).

Similar to other well-established health variables, such as obesity and lack of physical exercise, multiple longitudinal studies have shown that chronic stress increases the risk of developing Type 2 Diabetes (T2D). In addition, behavioral risk variables did not fully explain the observed associations, suggesting that physiological stress reactions have a direct role in the development of type 2 diabetes (28).

A biphasic plasma hormonal response of (nor) adrenaline and glucocorticoids (GCs) (cortisol in humans, corticosterone in rodents) is the ending point of the physiological stress response, which begins with the rapid activation of the SNS and continues with a more gradual and delayed reaction of the hypothalamic-pituitary-adrenal (HPA) axis. Hormones have an important role in maintaining homeostasis and facilitating behavioral adaptation to stress. They regulate several aspects of the neurological, immunological, cardiovascular, and metabolic systems that are relevant to type 2 diabetes. Circumstantial stress, which involves ongoing activation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis, can cause physiological disturbances that add up to "wear and tear" and heighten "allostatic load." The concept of "allostatic load" has made it possible to measure chronic stress using measurable physiological markers, which in turn has allowed researchers to find links between different stressors and the development of type 2 diabetes. There is strong evidence that chronic stress increases the likelihood of developing type 2 diabetes through inflammatory and cortisol-related dysregulations, which are markers of allostatic load (29,30). However, the exact pathophysiological processes underlying these connections have mainly eluded understanding. Many limitations need to be considered in order to expand current perspectives on the links between chronic stress and type 2 diabetes and to develop more mechanistic models.

1.5.1 Increased susceptibility to PONV and POCD in diabetic populations due to comorbidities and medication interactions.

The majority of patients experience nausea, vomiting, or retching within 24 hours after LSG, a condition known as postoperative nausea and vomiting (PONV). Without preventative antiemetic treatment, the incidence can reach 80%. Significant complications, such as a water-electrolyte imbalance and aspiration pneumonia, can arise from postoperative nausea and vomiting (PONV), which in turn prolongs hospital stays and increases healthcare expenditures. Previous studies have classified the factors that can cause nausea and vomiting after surgery into three groups: those that are specific to the patient (such as a history of gastrointestinal disorders, anxiety, infection, or a female gender), those that are associated with the anesthesia or pharmacology (such as opioids, volatile anesthetics, or nitrous oxide), and those that are surgical (such as the length of the procedure, the type of procedure, or the surgical technique). In adults, characteristics that increase the likelihood of postoperative nausea and vomiting (PONV) include being a female, not smoking, receiving opioids after surgery, being younger, and having a history of PONV or motion sickness (31–33). However, there might be more explanations for why obese individuals are more prone to PONV. Postoperative nausea and vomiting (PONV) is more common in bariatric surgery patients who are younger, do not smoke, have laparoscopic or robotic procedures that last more than an hour, and receive opioid analgesia before the procedure. Nausea and vomiting after surgery may be worsened by reduced stomach volume and impaired splanchnic perfusion caused by pneumoperitoneum, especially after laparoscopic sleeve gastrectomy.

Heart disease, high blood pressure, and high cholesterol are just a few of the comorbidities that are associated with diabetes mellitus. Antihypertensives, anti-hyperlipidemics, and antiplatelet medicines are commonly recommended alongside antidiabetic drugs, according to a global analysis of prescriptions for diabetic patients. High arterial blood pressure, or hypertension, affects about 70% of people with diabetes. The risk of getting hypertension is twice as high for people with diabetes as it is for people without the disease. Among diabetic patients, 41.5% were also administered medication for hypertension (34–36) and known to increase the risk of cardiovascular illnesses, dyslipidemia is often associated with diabetes. The risk of

cardiovascular problems can be reduced by the use of hypolipidemics, the most common of which being statins. Platelets are involved in hemostasis because they help produce thrombus. Atherogenesis, the process by which artery blockage and increased risk of ischemia occur, is heavily reliant on platelets. Therefore, it is essential to reduce the risk of ischemia in diabetes patients by including antiplatelet medicine.

1.5.2 The impact of ketamine on postoperative nausea, vomiting, and cognitive dysfunction

Neurocognitive alterations may occur during the perioperative period due to anesthesia, surgery, or other medical issues. Both postoperative delirium (POD) and cognitive dysfunction (POCD) can occur after surgery as a result of the procedure itself as well as micro- and macroemboli, blood loss, hypotension, hypoxia, cardiopulmonary bypass (CPB), and reperfusion damage. Within the first three days following surgery, a postoperative nausea and vomiting (POOD) range of 10% to 80% often develops. At six months or later, persistent impairment is observed in as many as 80% of elderly POD patients. Recovery at discharge is a mere 4%. Three months following heart surgery, the POCD rate in older individuals can be anywhere from 20% to 50%, and it can reach 55% in patients having other major surgeries (39).

PODS is based on empirical evidence. If administered to surgical patients, ketamine may reduce the likelihood of postoperative nausea and vomiting (POOD). An anti-nociceptive agent, ketamine is an NMDA antagonist that affects central sensitization and pain. Previous studies have demonstrated that ketamine, when administered intraoperatively under anesthesia, decreases pain, opioid use, and inflammatory markers following surgery. The hallucinogenic effects of ketamine have not prevented it from protecting against neurocognitive damage following surgery. Both people and animals benefit from ketamine's ability to decrease inflammation and postoperative delirium. Ketamine added to standard anesthetics may lower postoperative complications from cardiac surgery to 3% from 31% in the placebo group, according to recent studies. In addition to reducing inflammation after surgery, ketamine may safeguard the central nervous system (40). On the other hand, there was no discernible difference in outcomes between cardiac and non-cardiac surgeries in a large-scale trial that administered a single dosage of ketamine during induction. When used alone, ketamine has the potential to induce euphoria, confusion, impaired cognition, and problems with perception.

- To evaluate the efficacy of ketamine in reducing postoperative nausea, vomiting, and cognitive dysfunction in diabetic patients undergoing laparoscopic cholecystectomy.

CHAPTER 2

LITERATURE OF REVIEW

2.1 Introduction to Postoperative Complications

2.1.1 Postoperative nausea and vomiting (PONV),

Postoperative nausea and vomiting (PONV), which is defined as sensations of illness, throwing up, or retching following surgery, reportedly affects 12–38% of patients. Patient populations at increased risk for postoperative nausea and vomiting (PONV) include those who are younger, do not smoke, are female, and have a personal or family history of PONV or motion sickness (PONV prevalence up to 70-80% in these groups) (41,42). Pulmonary embolism, electrolyte and fluid imbalances, dehydration, increased patient physical stress, lengthier hospital stays, and increased medical costs are all potential consequences of PONV. A number of variables influence the likelihood of postoperative nausea and vomiting (PONV), including inhaled anesthetics, opioid administration both during and after surgery, intraoperative fluid infusion volume, anesthesia type and duration, and operation time. Several clinical investigations have shown that patients taking high dosages of opioids before surgery are at increased risk for postoperative nausea and vomiting. Despite advancements in prevention and therapy, over 30% of patients still experience postoperative nausea and vomiting (PONV) following thoracic surgery. Contrasted with the wealth of research on avoiding postoperative nausea and vomiting (PONV) in thoracic surgery, there is a dearth of research on opioid decrease (43).

A number of brain regions that regulate balance, breathing, eye movement, salivation, and vasomotor regulation are highly correlated with the vomiting center. The near proximity of these regions in PONV explains a number of physiological vegetative reactions, including salivation, sweating, frequent swallowing, pallor, tachypnea, tachycardia, arrhythmia, pupil dilation, and motion nausea. Nausea and vomiting during surgery can make patients less comfortable, cause release delays, and increase healthcare costs. Possible complications include electrolyte imbalance, dehydration,

wound dehiscence, hemorrhage, esophageal rupture, airway blockage, and aspiration pneumonia (44).

A complicated, persistent, and exceedingly unpleasant issue for anesthesiologists, PONV is one of the major and troubling morbidities linked to anesthesia and surgery. The overall incidence of severe, persistent postoperative nausea and vomiting (PONV) is estimated to be between 28 and 80 percent, with an estimated 18 percent of surgery patients experiencing this. When compared to countries like Ethiopia, which suffer from a lack of resources, Germany's 2.4 million PONV patients are expected to receive superior medical care annually. Postoperative nausea and vomiting (PONV) is 25% to 30% more common in surgical patients with American Society of Anesthesiologists (ASA) 1 or 2 risk levels compared to high-risk patients with ASA 3 or higher levels. Despite the widespread use of prophylactic antiemetics, postoperative nausea and vomiting (PONV) continues to be a significant concern. There are numerous factors that can increase the risk of postoperative nausea and vomiting (PONV), including age, sex, prior diseases, premedication, surgical procedure, anesthetic agents, analgesic medicines, duration of anesthesia, and postoperative complications (45,46).

2.2 Common surgical complications: cognitive impairment, vomiting, and nausea

When neurocognitive function decreases following surgery and anesthesia, it is referred to as "postoperative cognitive dysfunction" (POCD). This condition affects the central nervous system. Postoperative cognitive decline (POCD) is common in those aged 65 and up and is characterized by diminished abilities in memory, concentration, language fluency, orientation, and social skills after surgery. Since its inception, POCD has been the subject of extensive research; nonetheless, a definitive explanation remains unknown. Postoperative complications after surgery (POCD) result from an interplay of numerous variables, such as patient age, operation type, anesthesia approach, and pain severity (47,48). On top of that, POCD can linger for weeks or even years, which can make rehabilitation more difficult, hospital stays longer, mortality rates higher, patients and their families deal with more physical and mental health problems, and overall more burdensome. As the population ages and the economy improves, the use of anesthesia for surgical procedures is becoming more complicated to manage for patients who are getting older. The risk of cognitive impairment following surgery is higher in patients who are older. Because of this,

finding a way to avoid POCD and identify it has become a top priority. An analysis of POCD that delves into its epidemiology, risk factors, pathophysiology, and potential prevention strategies offers valuable insights into the future of prevention and therapy (49,50).

2.3 Epidemiology of POCD

Delirium can occur in hospitalized patients with common medical issues. Hospitalized elderly individuals with preexisting delirium make about 11-25% of the total. Incident delirium is between 29 and 31 percent more likely to occur in older persons admitted to the hospital without delirium. This distinction may hold significant weight in the context of general medical patients, as the effects of event delirium and frequent delirium are distinct. The emergency room is crucial to the healthcare of the elderly since it is the first point of contact for most hospital admissions (51). Among the more than 120 million people who visit emergency rooms in the US every year, 15% are 65 and older. Nevertheless, the epidemiology of delirium in EDs cannot be fully captured by these statistics (52).

Even though hospital and emergency department patient demographics overlap significantly, it is critical to use caution when applying study results to other settings. In sharp contrast to the lengthier hospital stays, patients examined in emergency rooms are frequently discharged the same day they come. Additionally, patients are frequently enrolled for inpatient research within the initial two to three days of hospitalization, which may lead to bias as a consequence of inaccurate classification. The patient's delirium level during enrollment can be influenced by their history of delirium in the emergency room. For instance, patients who were deemed non-delirious before admission to the hospital can have had delirium while admitted to the emergency department. The reason behind this is that delirium might go away on its own in 20-51% of cases within a day (18).

2.3.1 Epidemiology of delirium in the Emergency department

Emergency room visits from the elderly account for 8-10% of cases of delirium. Studies that have examined delirium in the emergency room have had notable drawbacks, though. Most studies conducted in emergency departments only examine

delirium at a single point in time, making it impossible to predict the incidence of recurrent delirium among patients. One prominent cause of incident delirium in emergency rooms is the excessive use of psychoactive medicines, such as benzodiazepines and opioids. More study is required to establish the frequency of delirium in emergency departments.

Even though older individuals make up more than half of the emergency department's patient demographic, nothing is known about the prevalence of delirium among these patients when they are released. According to Han et al., 19% of the older patients exhibited delirium symptoms even after being released from the emergency department. Furthermore, Naughton et al. found that 13% of the elderly patients who were discharged from the emergency hospital exhibited symptoms of delirium. Research on the short- and long-term consequences of releasing delirious patients is urgently needed in light of a study that found a link between delirium upon release and higher 6-month mortality rates (54,55).

2.3.2 Epidemiology of postoperative delirium

The same risks as other patient groups are related with postoperative delirium, including longer hospital admissions, worse functional decline, longer cognitive impairment, and death. Although postoperative delirium (POD) is prevalent, the rates reported by various research can differ substantially. This is due to the fact that there isn't a well-defined boundary between the emergence, post-anesthesia care unit, and postoperative day, and there are also varying criteria for diagnosing delirium. The under-diagnosis of hypoactive subgroups is likely due to the fact that no validated delirium-monitoring approaches exist and that previous research on POD has concentrated on hyperactive delirium (56). Studies have shown that exposure to sedatives and analgesics, co-morbidities, and the severity of surgical trauma all raise the risk of postoperative delirium (POD).

The correlation between surgery type and delirium risk is a novel vulnerability risk factor in the postoperative context. The incidence of postoperative delirium (POD) increases with surgical risk, as shown by the following statistics: 12% for otolaryngological surgery, 13% for general surgery, 29% for aortic surgery, 50% for major abdominal surgery, and 51% for cardiac surgery. Factors such as longer surgical

length, greater blood transfusion rates, emergency surgery versus elective surgery, longer surgical procedures, and open surgery versus endovascular surgery all contribute to an elevated surgical burden and an increased risk of postoperative delirium (POD) (57). There is uncertainty regarding the role of off-pump coronary bypass in preventing or increasing the risk of postoperative delirium (POD) in cardiac surgery, in contrast to the known risks of protracted cardiopulmonary bypass, valve surgery, and balloon pump support.

2.4 Risk factors of POCD

2.4.1 Age

Postoperative cognitive dysfunction (POCD) is a growing concern among older persons undergoing surgery, as the surgical patient population is clearly getting older in clinical settings. According to studies, approximately 30% of younger patients and 40% of older patients experience postoperative constipation. I find it somewhat surprising that just 5% of younger patients still exhibit symptoms of POCD three months following surgery, in contrast to 12.7% of older patients (58). Because of natural aging processes and the possibility of respiratory, cardiovascular, and cerebrovascular diseases, the elderly have a much lower anesthesia tolerance. This indicates that POCD is more common in the elderly.

2.4.2 Types of surgery

One frequent way that the elderly deal with the joint problem known as osteoarthritis is by undergoing arthroplasty treatments. Even while these procedures increase joint function and pain reduction, postoperative cognitive dysfunction (POCD) is more likely with them than with general surgery. The increased risk is a result of the lengthier surgery times, higher levels of surgical stress, and the possibility of fat embolism. Coronary artery disease (CAD) is a common and potentially fatal illness that has been increasing in both prevalence and death rates worldwide in recent years. Coronary artery bypass grafting is the most effective treatment for coronary artery disease, although it comes with a higher risk of cognitive dysfunction after surgery, especially when cardiopulmonary bypass is involved. Postoperative cerebral hemorrhage (POCD) can occur due to insufficient blood flow to the brain following heart surgery, inflammation, or cerebral microembolism. The cardiopulmonary bypass

machine (CPB) has the potential to introduce microemboli into the cerebral circulation during a CPB procedure, including thrombi, air bubbles, and adipose tissue. Furthermore, atherosclerotic plaques can be dislodged during surgery, leading to embolism, if the aorta is obstructed. Investigators discovered tiny emboli in the brains of patients who died following CABG-CPB (coronary artery bypass grafting with cardiopulmonary bypass) (59). Head MRI studies show that more than 50% of CABG patients experience brain microembolic infarction, a condition that leads to minor neurological deficits. Scientific evidence shows that immunological responses occur during cardiopulmonary bypass when blood components come into touch with synthetic materials. The activation triggers systemic inflammatory responses, which can cause organ damage after reperfusion. Some inflammatory chemicals from the periphery can pass the blood-brain barrier and cause inflammation in the central nervous system and postoperative cognitive dysfunction (POCD) (60).

2.4.3 Types of anesthesia

The anesthesiologist will advise either general or intravertebral anesthesia based on the surgery's requirements. Prior studies found no statistically significant difference in the rates of postoperative complications (POCD) between individuals who had knee arthroplasty under general or intravertebral anesthesia at one week and six months following the procedure. Each of the three groups of patients undergoing hip arthroplasty had a different sedative and spinal-epidural block: midazolam, dexmedetomidine, and propofol. Compared to the groups given midazolam or dexmedetomidine one week after surgery, those given propofol had a significantly lower incidence of postoperative confusion disorder (POCD). The combination of midazolam and isoflurane is a common anesthetic method. A rat anesthetic trial with this combination revealed extensive neuronal death and disrupted hippocampal connections, which could indicate a potential impairment in cognitive function. Compared to procedures utilizing inhalation anesthesia with isoflurane, a meta-analysis of 28 RCTs found that intravenous anesthesia with propofol was linked with a decreased prevalence of Postoperative Cognitive Dysfunction (POCD)(61).

2.4.4 Pain management

The likelihood of wound infection and the amount of stress experienced during the operation are two of the many potential causes of postoperative pain, which is a major concern for many patients. This is why, following surgery, patients are prescribed antibiotics to avoid infection and analgesia pumps to alleviate pain. Patients who reported using patient-controlled analgesia pumps independently following surgery had a higher incidence of postoperative cognitive dysfunction (POCD). Compared to patients who received intravenous opioids via a patient-controlled analgesia device, those who were given oral postoperative analgesics were far less likely to develop postoperative cognitive dysfunction (POCD)(62,63). Su et al. found that dexmedetomidine, when added to the standard postoperative analgesics, reduced postoperative pain and improved cognitive function. Psychological functions including memory, focus, and processing speed may also be impaired in those who suffer from chronic pain, according to pain meta-analyses.

2.4.5 Education level

A decreased prevalence of POCD may be associated with higher levels of education. Synapse function and neural reserve are both enhanced in this educated group since their brains are continually working on mentally demanding tasks. Patients experiencing postoperative cognitive impairment due to hippocampus injury may benefit from a strong brain reserve. Generally speaking, the pathological alterations caused by neurodegenerative illnesses are more easily tolerated by patients with greater levels of education. Additionally, those who have a high level of cultural reserve have a slower rate of aging and cognitive loss (64).

Although patient consent isn't always simple to come by, neuropsychological assessment is the gold standard for establishing POCD. Therefore, a sensitive and precise biomarker for POCD prediction is urgently needed. After surgery, surgeons and anesthesiologists may take additional measures to reduce the chances of postoperative cognitive dysfunction (POCD) in patients who are deemed high-risk. Recent studies have highlighted mitochondrial metabolic dysfunctions, aberrant tau protein modification, neuronal death, poor synaptic plasticity, chronic pain, and inflammation of the central nervous system as factors in the pathophysiology of POCD. Cognitive training and specific medications have been shown in multiple

studies to reduce POCD (65). When administered at the appropriate time, these therapies can lessen the frequency of POCD.

2.5 Role of Ketamine in management of PONV in Laparoscopic surgery

One time-tested approach for managing post-operative pain in patients undergoing spinal surgery is intravenous opioid-based patient-controlled analgesia, or IV-PCA.¹ Despite the excellent analgesic impact, opioids increase the incidence of postoperative nausea and vomiting (PONV), which frequently worsens patients' postoperative course. The likelihood of experiencing nausea and vomiting after surgery (PONV) is increased by a number of factors, such as being a female, having a history of motion sickness or PONV, and not smoking. When three of these risk factors were present, the reported incidence of PONV increased by 61%, and when four of them were present, it increased by 79% (66,67). There are a number of pharmacologic drugs that have been effective in preventing PONV.³ Prevention of opioid-related side effects, such as PONV, has been shown to be an achievable goal in studies that used a multimodal regimen including anti-emetic medicines, non-steroidal anti-inflammatory medications, or tramadol.^{4 5} Postoperative nausea and vomiting (PONV) refers to the combination of symptoms of nausea, vomiting, and retching that patients may experience in the postanesthesia care unit (PACU) or in the first 24-48 hours after surgery. As a group, symptoms like nausea and vomiting that occur after leaving a healthcare facility or surgical center are called postdischarge nausea and vomiting (PDNV). In addition to being a distressing side effect for the patient, postoperative nausea and vomiting (PONV) can cause a host of other problems, including: dehydration, acid-base imbalance, hypoxia, esophageal rupture, increased intracranial pressure, suture rupture, wound dehiscence, bleeding, postoperative anxiety, fatigue, prolonged hospital stay, increased medical expenses, and prolonged time in the postoperative care unit (PACU). Postoperative nausea and vomiting, or PONV/PDNV, can last anywhere from nine to twelve hours and is a common reason individuals dislike surgery. The hospital can reap financial benefits from PONV prevention when a well-planned multimodal program is implemented based on patient and procedural risk factors (70).

2.6 Risk factors for PONV and PDNV

In order to provide the most effective antiemetic prophylaxis to those who are most in need of it, it is necessary to identify risk factors for PONV. the range of 21–26. The frequency of nausea and vomiting following surgery depends on a number of factors, including the patient, the anesthesia, and the procedure itself. A patient's unique characteristics include being female (odds ratio [OR] 2.57), not smoking (OR 1.82), having a history of postoperative nausea and vomiting (PONV) or motion sickness (OR 2.09), and being under 50 years old (OR 1.79 in the post-anesthesia care unit [PACU] and OR 2.17 for postoperative delayed nausea and vomiting [PDNV]). 27 times, 37 times, 38 times. Prepubescent girls do not have a higher risk of postoperative nausea and vomiting (PONV) compared to boys. Very little is known about the likelihood of POV/PONV in children who are exposed to secondhand smoke in the literature. Children are more likely to experience postoperative nausea and vomiting (PONV) or postoperative vomiting (POV) if they have had it before during surgery or if they have a family history of the condition. Pain was found to be a contributing factor in cases of postoperative nausea and vomiting (PONV) that persisted after discharge, according to research by Chandrakantan et al. and Kocaturk et al. Patients under the age of 18 who were impaired were more likely to experience postoperative nausea and vomiting (PONV), according to Turgut et al. (74) as well. While some studies have found a correlation between age and postoperative nausea and vomiting (PONV) in pediatric patients, others have found no such correlation. Among these studies, 29, 43–45 found that younger children were less likely to experience PONV.

2.7 Efficacy of intraoperative subanesthetic dose of ketamine/esketamine in preventing postoperative cognitive dysfunction

As a common side effect of anesthesia, postoperative cognitive dysfunction (POCD) affects about 12% of patients and can reach 41.4% in older patients who undergo surgery while they are in the hospital. While the exact nature of postoperative cognitive decline (POCD) is still up for debate, one common description is a decline in cognitive abilities compared to the patient's level of functioning before surgery. Cognitive impairments such as memory loss, mood swings, disorientation, and sleep problems

are the most common symptoms of postoperative cognitive dysfunction (POCD), which can last for weeks or months after surgery. In the aged in particular, this syndrome is associated with increased death rates, longer hospital stays, slower recoveries, and unexpected consequences. On top of that, some people deal with POCD for a long time, maybe years, and eventually develop permanent brain damage (75). Age, cognitive impairment, surgery type, intraoperative hypotension, anesthesia depth and duration, pain management, inflammatory biomarkers, and other risk factors are among the many that can arise during the perioperative period and increase the likelihood of postoperative complications. One of the main causes of postoperative chronic pain (POCD) is inflammation in the brain after surgery. Unfortunately, there are currently no effective ways for preventing or treating POCD, and the underlying pathophysiology is still unclear. As a result, POCD prevention is becoming a major concern.

Intraoperative anesthetic and supplemental perioperative analgesia are the main uses of the versatile ketamine, which has seen widespread use since the 1970s. Its beneficial cardiovascular qualities and ability to decrease glandular production make it a common choice for administration to burn victims and pediatric patients. 18 The psychotic symptoms may be worsened by the sympathomimetic effects of ketamine, which include increased sympathetic activity, cardiac contractility, and heart rate. Thus, individuals with hyperthyroidism, severe preoperative psychiatric problems, hypertension, or major cardiovascular sickness should be cautious(77). Although ketamine's effectiveness in preventing POCD has been debated, it has gained some traction in recent years. There have been 22 conflicting results that show intraoperative ketamine/esketamine may not help prevent POCD, even though many clinical trials have shown that it reduces the incidence of POCD. The range is from 23–25

There may be a correlation between the method of administration and the therapeutic effects of ketamine/esketamine. Our meta-analysis includes studies in which the intervention group received either ketamine/esketamine monotherapy or a combination of the two plus an unproven medication for the prevention of POCD. Thus, ketamine/esketamine administration alone may not be effective in preventing POCD; however, multiple studies suggest that ketamine/esketamine combined with other pharmacological agents may be beneficial. A randomized controlled trial with

100 participants showed that postoperative cognitive dysfunction (POCD) was significantly lower in the group that received a single dose of ketamine during heart valve replacement surgery (20%) compared to the group that received a combination of etomidate and ketamine (6%). A total of 42 Postoperative cognitive dysfunction (POCD) was less common in the combination group that received both haloperidol and ketamine than in the control group, according to a separate randomized controlled trial that included 182 patients. However, when given alone, haloperidol and ketamine had no better impact on POCD than the control group (15.6% and 21.3% versus 13.6%, respectively). Twenty-four To confirm that these combinations are safe and helpful in avoiding POCD, more research is needed (78–80).

2.8 Ketamine in Diabetic Populations

The symptoms of major depressive disorder (MDD) are common, intense, and long-lasting; they are also associated with an increased risk of suicide attempts. Major depressive disorder (MDD) is characterized by changes in metabolic markers, weight, eating habits, and hunger. Metabolic dysfunction due to steatotic liver disease is one of several medical disorders characterized by impaired insulin signaling; existing cross-sectional and longitudinal studies show a strong bidirectional relationship between MDD and these conditions (81).

In addition, there is a correlation between the intrinsic risk of type 2 diabetes in MDD and several psychiatric drugs, such as conventional antidepressants, which increases the possibility of serious metabolic problems. Major depressive disorder (MDD) is characterized by abnormalities in glucose-insulin homeostasis, which in turn cause and worsen abnormalities in a number of psychopathological domains (such as anhedonia and overall cognitive performance) and increase the likelihood that antidepressants will have no effect. Thus, it is crucial to conduct both short- and long-term trials to better understand the effects of psychotropic medications on metabolic parameters in order to advance the field of research and development for new treatments for Major Depressive Disorder (82).

2.9 Specific challenges in managing diabetic patients during anesthesia.

An established method for managing pain after spinal surgery is intravenous patient-controlled analgesia (IV-PCA), which is based on opioids.¹ Opioids provide better analgesic effects, but they also increase the risk of postoperative nausea and vomiting (PONV), which can make patients' recoveries from surgery more difficult. In addition to the use of opioids after surgery, being female, having a history of motion sickness or postoperative nausea and vomiting (PONV), and not smoking are also major risk factors that increase the likelihood of PONV. The presence of three or four of these risk variables was associated with an increase in the reported incidence of PONV to 61% and 79%, respectively: 85. To prevent PONV, various pharmaceutical drugs have been used singly or in combination. Array of three Researchers have shown promising results in reducing opioid-related side effects, such as postoperative nausea and vomiting (PONV), when using a multimodal approach that includes non-steroidal anti-inflammatory drugs (NSAIDs) or tramadol in addition to anti-emetic medications. Four The anesthetic ketamine blocks the effects of the neurotransmitter N-methyl-D-aspartate (NMDA). Ketamine, when administered at subanesthetic doses, blocks hyperalgesia, acute opioid tolerance, and central sensitization. Six A large body of research has investigated the use of ketamine in conjunction with opioids to alleviate pain immediately following surgery. Some of these trials have shown promising results, including a reduction in the occurrence of postoperative nausea and vomiting (PONV) and an opioid-sparing effect. Having seven A total of nine However, previous studies have shown a lot of diversity and conflicting findings. In addition, not a single trial focused on reducing the occurrence of PONV; this is especially concerning for high-risk patients, for whom the benefits of opioid-based IV-PCA may be rendered useless by the presence of PONV (86,87).

2.10 Laparoscopic Cholecystectomy and Its Anesthetic Implications

2.10.1 Overview of laparoscopic cholecystectomy: surgical procedure and outcomes.

The goal of minimally invasive laparoscopic surgery is to achieve the same effective treatment with less patient discomfort. Reduced postoperative pulmonary complications, shorter hospital stays, faster recovery, speedier return to normal activities, and less surgical discomfort are just a few of the many reasons why this

technique is so popular. Inflating gas into the abdominal cavity is a necessary step in the operating technique to make the surgery easier. The prescribed intra-abdominal pressure (IAP) ranges from 10 to 15 mmHg. The non-combustible, highly soluble, and quickly cleared gas known as carbon dioxide (CO₂) has many practical applications. The problem with CO₂ is that it can cause hypercapnia and respiratory acidosis if it is absorbed (91).

2.10.2 Anesthetic considerations for diabetic patients in laparoscopic surgery.

In China, 10.9% of the population had diabetes, while 35.7% had prediabetes. Diabetes complications such as peripheral neuropathy, kidney damage, vascular disease, limb death, and cardiovascular disease manifest in the later stages of the disease. Mortality associated with a previous MI, stroke, or diabetes was similar across all circumstances. Individuals with multi morbidity have a substantially shorter life expectancy due to the higher mortality risk associated with any combination of these disorders. Life expectancy decreased beyond the age of 40 for those who had diabetes, a myocardial infarction, or a stroke. Significant abdominal procedures, including as liver, gastrointestinal, and biliary surgeries, are becoming more common for persons with diabetes, who often need surgical interventions throughout their lifetimes (92).

CHAPTER 3

METHODOLOGY

1. Study Design

In this observational cross-sectional investigation, diabetic patients undergoing elective laparoscopic cholecystectomy were evaluated for cognitive impairment, postoperative nausea and vomiting (PONV), and the effects of ketamine.

2. Clinical Setting

This study focused on diabetic patients scheduled for elective laparoscopic cholecystectomy and was conducted in the Anesthesia Department of Mayo Hospital Lahore. In order to evaluate postoperative vomiting, nausea, and cognitive function, the clinical setting included preoperative, intraoperative, and postoperative care zones.

3. Study Duration

The duration of this study was four months. Demographic information, clinical characteristics, and outcome metrics such as postoperative nausea, vomiting, and cognitive evaluations were painstakingly gathered before, during, and after the operation.

4. Sample Size

One hundred sixty-three diabetic individuals who opted for laparoscopic cholecystectomy were included in the research. With a 95% confidence interval, a 5% margin of error, and an anticipated prevalence of 26% for the outcome variable (Postoperative Cognitive Dysfunction, POCD), the sample size was computed using Open Epi, a sample size calculator.

5. Sampling Technique

A consecutive non-probability sampling procedure was used to select the participants. In order to reach the calculated sample size, we invited for inclusion all eligible patients who were scheduled for elective laparoscopic cholecystectomy during the study period.

6. Selection Criteria

6.1 Inclusion Criteria

- Patients with diabetes aged 18 to 75 years.
- Planned for elective laparoscopic cholecystectomy.

- Capable of granting informed consent.
- Preoperative cognitive assessments indicate baseline cognitive performance is within normal norms.

6.2 Exclusion Criteria

- Individuals with a history of significant psychiatric or neurological illnesses.
- Individuals with contraindications to dexmedetomidine.
- Patients receiving emergency cholecystectomy.
- Patients exhibiting considerable hemodynamic instability or need acute care prior to surgery.
- Women who are pregnant or lactating.

7. Data Collection Procedure

Qualified diabetic patients scheduled for elective laparoscopic cholecystectomy had their informed consent obtained before baseline demographic and clinical data were collected. All of the following were included: gender, age, height, weight, number of years with diabetes, and hemoglobin A1c levels. Each patient's cognitive performance was assessed using established assessment tools, such as the Mini-Mental State Examination (MMSE), to establish a cognitive baseline. The use of conventional clinical equipment also allowed for the measurement of baseline hemodynamic markers including pulse rate and blood pressure. The evaluation of changes both before and after surgery relied heavily on these first assessments. To guarantee airway security during general anesthesia, all patients in this trial were intubated with an endotracheal tube. Continuous assessment of vital signs, including heart rate (HR), and assurance of adequate peripheral venous access for medication administration were both performed by means of a multifunctional monitor. Using a noninvasive blood pressure meter, the patient's systolic and diastolic readings were recorded to demonstrate that their hemodynamic status remained stable during the surgery.

A critical trio of medications were administered during the routine induction of anesthesia. The patient was put to sleep with propofol (1 mg/kg), given an opioid analgesic (0.5 µg/kg) for pain relief, and given atracurium (0.15 mg/kg), a muscle relaxant, to make sure the intubation went smoothly by relaxing the muscles in the body. Once intubation was effective, the patient's respiration was regulated by an anesthetic machine to ensure adequate ventilation during the surgical process. Following standard procedures for protecting the lungs during anesthesia, the

equipment was fine-tuned to deliver a tidal volume (VT) of 6-12 mL/kg of body mass, a respiratory rate (RR) of 12 breaths/min, and an inspiratory-expiratory ratio of 1:2. During the period of maintenance of anesthesia, a short-acting opioid called remifentanyl was given for continued analgesia, and a continuous intravenous infusion of propofol (75 µg/kg/min) was used to keep the patient asleep. To keep muscles relaxed throughout surgery, cisatracurium (0.03 mg/kg) was administered intravenously on an as-needed basis. The anesthetic medications were fine-tuned to keep the patient asleep, reduce pain, and relax during the procedure, allowing for a risk-free surgery.

Patients underwent intravenous sedation with midazolam (0.05 mg/kg) during the anesthetic induction phase, followed by general anesthesia with propofol (2-3 mg/kg). Opioid analgesia was achieved with fentanyl (0.4-0.6 µg/kg), and muscle relaxation was achieved with cis-atracurium besylate (0.2 mg/kg). Following this, a two-lumen bronchial tube was inserted to secure the airway and allow for one-lung ventilation, which is standard for laparoscopic procedures like cholecystectomy. Then S-ketamine were given a 0.5 mg/kg intravenous bolus dose of S-ketamine just after they were anesthetized. S-ketamine was chosen because of its possible benefits in reducing postoperative symptoms such vomiting, nausea, and cognitive impairment while simultaneously improving pain relief during surgery.

Strict control of respiratory parameters was required because the surgical procedure required one-lung ventilation. The patient's ideal body weight was used to calibrate the tidal volume, which was 6-8 mL/kg. To ensure safe ventilation, the peak airway pressure was kept under 30 cmH₂O. By adjusting these parameters, the surgeon can lessen the likelihood of ventilator-associated lung harm. An intravenous bolus injection of palonosetron (0.075 mg), a medication used to prevent postoperative nausea and vomiting (PONV), was administered to all patients before the surgery began.

For the purpose of maintaining anesthesia during the surgery, the patients received continuous infusions of remifentanyl (0.1-1.0 µg/kg/min), propofol (4-8 mg/kg/h), and S-ketamine (0.25 mg/kg/h). The patient's vital signs and the needs of the surgery dictated the adjustments to the dosages. All the patients were given ketamine boluses and ketamine infusions to maintain sedation and analgesia during laparoscopic surgery.

Analgesia adequacy for monitoring and treating intraoperative pain was evaluated using the surgical volume tracing index (SPI). To make sure the patient is comfortable without being overly sedated, this index can be used to determine the appropriate amounts of anesthetic and analgesia. An increase in the remifentanyl dosage would be required if the SPI score was high (indicating insufficient analgesia), whereas a decrease in the score (indicating excessive analgesia) would call for a decrease in the infusion rate. Additionally, to prevent overactive muscles during the treatment, cis-atracurium besylate was given when needed to further calm the muscles. In order to avoid any potential postoperative complications, the S-ketamine was stopped 15 minutes before the surgery was to be finished.

The control of fluid balance was crucial, since it influences postoperative nausea and vomiting (PONV). In order to avoid postoperative complications related to fluid overload, the study used a limited fluid management strategy with a crystalloid-to-colloid ratio of 2:1. A number of critical parameters were constantly tracked throughout the operation, including the patient's pulse, respiration rate, temperature, end-tidal CO₂, mean arterial pressure, electrocardiogram (ECG), volume of fluid infusion, output of urine, and bispectral index (BIS). Particularly with postoperative nausea and vomiting (PONV) and cognitive dysfunction, these procedures are critical for keeping patients stable during surgery and for identifying any early problems or adverse events that can affect recovery.

Cognitive assessments were administered to patients using the same instruments used before surgery at predetermined intervals including 2, 4, 6, and 8 hours postoperatively. In the event that postoperative cognitive dysfunction (POCD) occurred, these assessments helped to detect it. In order to track changes and identify any delayed hemodynamic instability, postoperative hemodynamic measures were recorded at these intervals. In order to assess the level of sedation and cognitive status of patients after surgery, the Richmond Agitation-Sedation Scale (RASS) and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) were consistently recorded at regular intervals. At 2-hour intervals for the first 8 hours after surgery, RASS assessments were carried out. Medical experts documented the RASS scores after assessing the agitation and reactivity of their patients on a defined scale ranging from -4 (unarousable) to +4 (combative). Regular assessments like these let doctors keep tabs on their patients' sedation levels and make necessary adjustments to their dosages quickly.

At 2,4,6, and 8 hours after surgery, CAM-ICU assessments were repeated at regular intervals. Delirium was determined by the CAM-ICU using the following criteria: altered levels of awareness as indicated by the prior RASS score; sudden onset or fluctuating mental state; inattention; disordered thinking. The CAM-ICU was administered by qualified evaluators who used organized tasks and evaluations to gauge the cognitive function and delirium symptoms of the patients. Quick action and better patient outcomes were made possible by these evaluations, which were critical for the early detection and treatment of postoperative delirium. Also documented were any problems or unfavorable consequences that may have occurred after the operation. The purpose of the data analysis was to determine whether ketamine improved perioperative outcomes. To ensure accuracy and privacy, all data were recorded in a safe, standardized format.

8. Data Analysis

We used SPSS (Statistical Package for the Social Sciences) to analyze the collected data. We used descriptive statistics like means, standard deviations, and frequencies to summarize demographics, perioperative variables, and outcomes like hemodynamic stability and postoperative cognitive dysfunction (POCD). Using appropriate statistical methods, such as t-tests for continuous variables and chi-square tests for categorical variables. To assess the effects of ketamine on patients receiving ketamine on account for any potential confounding variables, multivariate regression models were used. A p-value less than 0.05 was set as the cutoff for statistical significance. To help with understanding and discussing the results, tables and figures were used to illustrate the data.

CHAPTER 4

RESULTS

In this study the results have shown that the gender distribution in the group of 163 patients was nearly equal, with 52.1% men and 47.9% women. The majority of patients were 40–49 years old (30.7%) and 50–59 years old (33.7%). In education category 42.9% had completed high school, 30.7% had an associate, and 26.4% had a bachelor's degree. The majority of individuals fell within the 70–80 kg weight range, while 42.9% of the total falling within the 160–170 cm height range. According to their body mass index (BMI), a significant number were classified as overweight (42.9%) or obese (32.5%). About 58.3% of the population had type II diabetes, making it the most common form of the disease. For 38.7 percent of the people, the diagnosis lasted longer than 10 years. Overall, HbA1c readings ranging from 6.5% to 7.5% and were seen in 42.9% of the population. Nearly half of the patients (41.1%) underwent procedures that lasted one to two hours, and a majority of those patients (73.6%) experienced minimal blood loss (less than 100 ml) throughout the operation. Over half of the patients (55.2%) with healthy kidneys maintained fasting blood glucose levels < 130 mg/dl. Although a small percentage of individuals displayed significant abnormalities, 79.8 percent of liver function tests came within the normal range.

Table 4.1 Demographic characteristics (n=163)

Variable	Category	Frequency (n=163)	Percentage (%)
Gender	Male	85	52.1
	Female	78	47.9
Age Group (years)	30-39	20	12.3
	40-49	50	30.7
	50-59	55	33.7
	60+	38	23.3
Occupation	Teacher	40	24.5
	Nurse	30	18.4
	Retired	35	21.5
	Office Worker	25	15.3
	Other	33	20.2

Education Level	High School	70	42.9
	Diploma	50	30.7
	Bachelor's Degree	43	26.4
Height (cm)	< 160	40	24.5
	160-170	70	42.9
	> 170	53	32.5
Weight (kg)	< 70	60	36.8
	70-80	70	42.9
	> 80	33	20.2
BMI Category	Normal (18.5 - 24.9)	40	24.5
	Overweight (25 - 29.9)	70	42.9
	Obese (30 and above)	53	32.5
Type of Diabetes	Type I	60	36.8
	Type II	95	58.3
	Gestational	8	4.9
Duration of Diabetes	< 5 years	40	24.5
	5-10 years	60	36.8
	> 10 years	63	38.7
Latest HbA1c Level	< 6.5%	50	30.7
	6.5% - 7.5%	70	42.9
	> 7.5%	43	26.4
Operation Duration	< 1 hour	60	36.8
	1-2 hours	80	49.1
	> 2 hours	23	14.1
Inter operative Blood Loss	< 100 ml	120	73.6
	100-200 ml	30	18.4
	> 200 ml	13	8
Fasting Blood Sugar (FBS)	< 130 mg/dL	90	55.2

	130-180 mg/dL	50	30.7
	> 180 mg/dl	23	14.1
Renal Function Test (RFT)			
	Normal	120	73.6
	Mildly Abnormal	30	18.4
	Moderately Abnormal	13	8
Liver Function Test (LFT)			
	Normal	130	79.8
	Mildly Abnormal	25	15.3
	Severely Abnormal	8	4.9

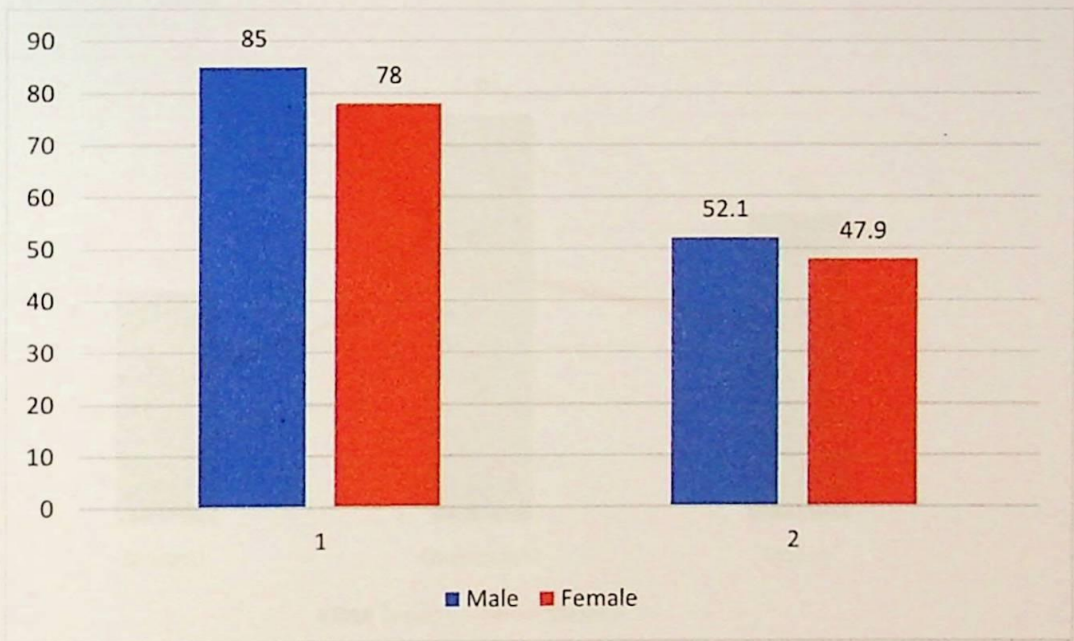


Figure 4.1 Gender Distribution of Patients

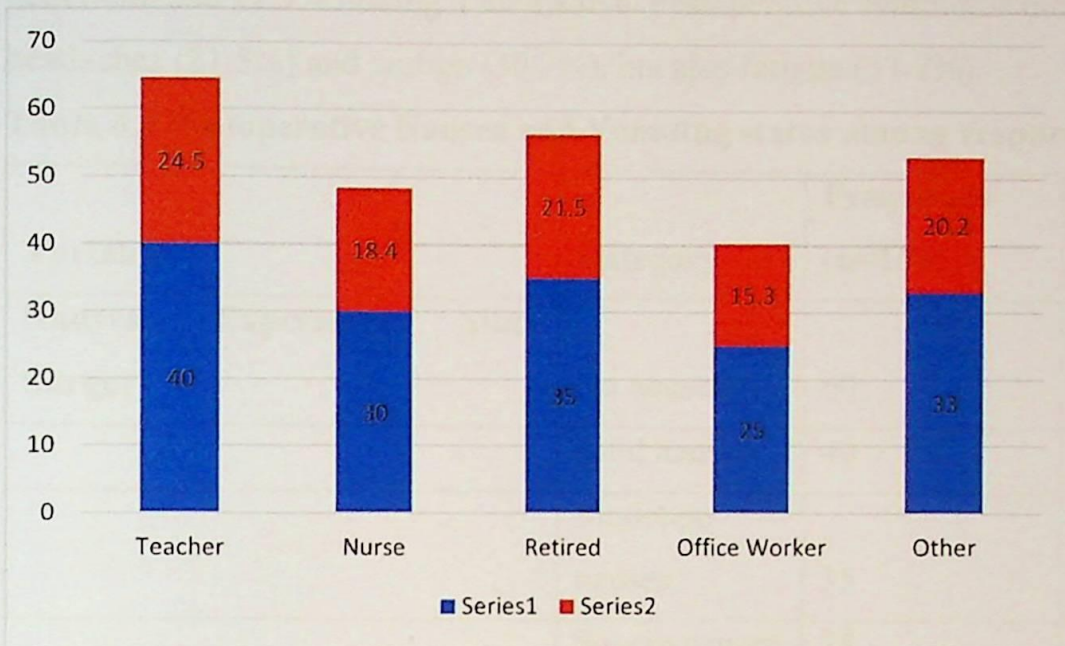


Figure 4.2 Occupation distribution

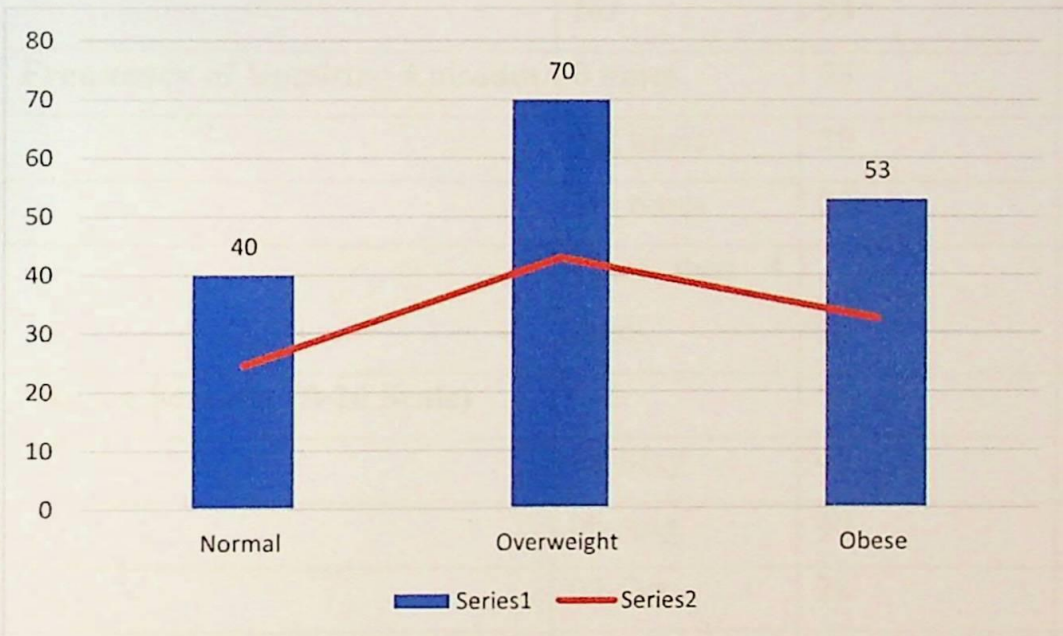


Figure 4.3 BMI Distribution

Of the 163 patients, 36.8% had absolutely no nausea following surgery, 25.5% moderate sickness, 21.5% severe nausea, and 17.2% absolutely no nausea at all. Among the 42.9% of patients who experienced vomiting, the frequency of episodes varied: 57.1% had no vomiting at all, 18.4% had one or two episodes, and 12.3% had three, four, or more episodes. From 0 to 10, 30.7% of individuals assessed the level of nausea as 0-2, and 17.2% as severe (9-10). Within the first two to six hours following surgery, 42.9% of patients had nausea or vomiting. Nearly half of individuals who took medicine for these symptoms had some improvement, with 37.5% finding it

beneficial and 12.5% finding it ineffective. Postoperative symptoms included not only headaches (21.5%) and vertigo (30.7%), but also fatigue (33.7%).

Table 4.2 Postoperative Nausea and Vomiting status among respondents

Variable	Category	Frequency (n=163)	Percentage (%)
Nausea Experience Since Surgery	No nausea	60	36.8
	Mild nausea	40	24.5
	Moderate nausea	35	21.5
	Severe nausea	28	17.2
Vomiting Since Surgery	Yes	70	42.9
	No	93	57.1
Frequency of Vomiting Episodes	0 times	93	57.1
	1-2 times	30	18.4
	3-4 times	20	12.3
	More than 4 times	20	12.3
Nausea Severity (0-10 Scale)	0-2	50	30.7
	03-May	45	27.6
	06-Aug	40	24.5
	09-Oct	28	17.2
Timing of Nausea/Vomiting After Surgery	0-2 hours	45	27.6
	2-6 hours	70	42.9
	6-12 hours	35	21.5
	12-24 hours	25	15.3
Medication for Nausea/Vomiting	Yes	80	49.1
	No	83	50.9
Effectiveness of Medication	Not effective	10	12.5 (of 80)
	Somewhat effective	25	31.3 (of 80)
	Effective	30	37.5 (of 80)

	Very effective	15	18.8 (01.80)
Other Postoperative Symptoms Experienced	Dizziness	50	30.7
	Headache	35	21.5
	Fatigue	55	33.7
	Other	23	14.1

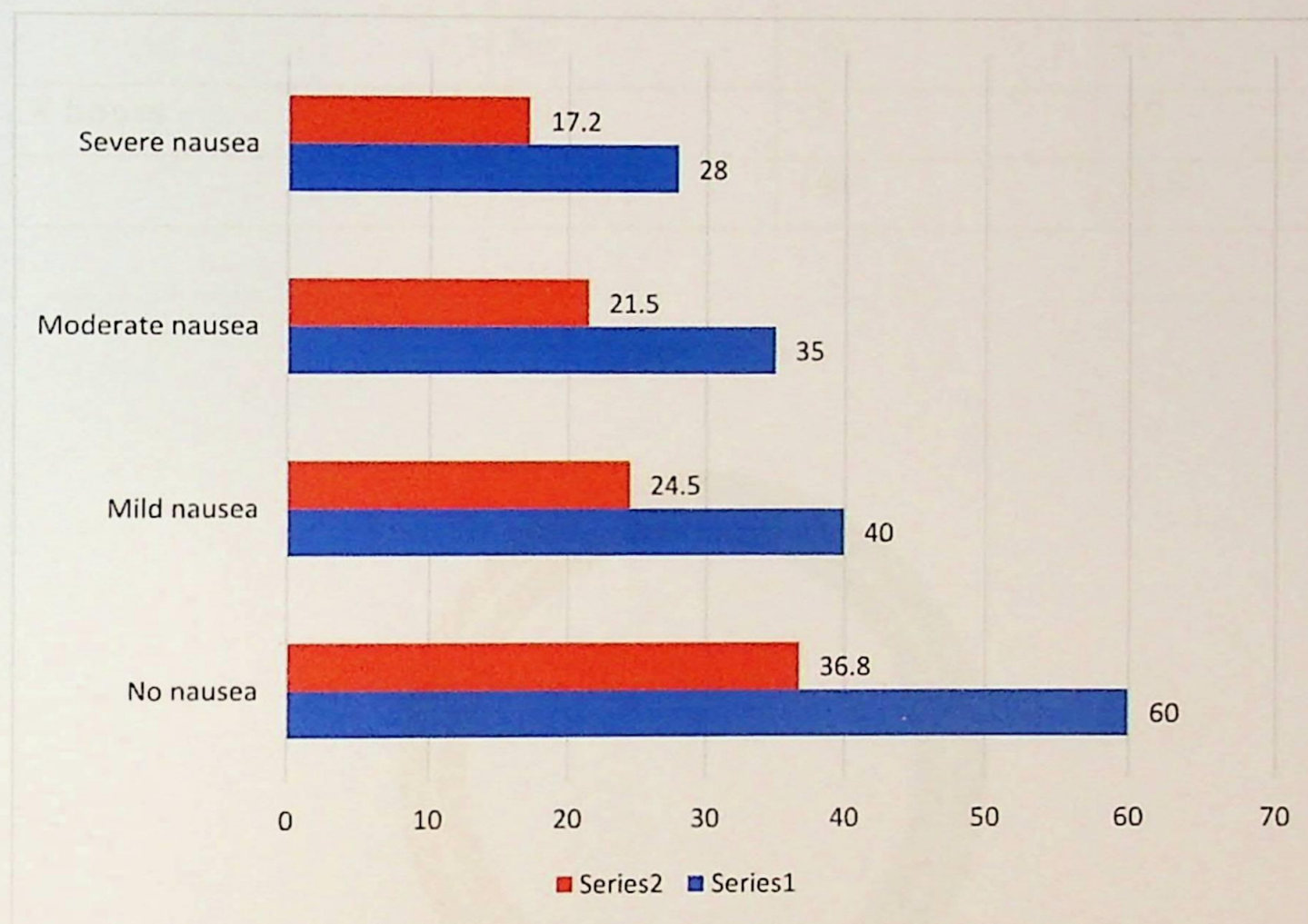


Figure 4.4 Nausea Status

This study of 163 participants found that the rate of delirium decreased as the period after surgery passed. After two hours of operation, just 18.4% exhibited delirium symptoms, while 81.6% showed no symptoms. Fifteen percent of patients experienced delirium by the end of the fourth hour, while eighty-four percent did not. At 6 hours, 87.7 percent of patients still showed no symptoms of delirium, while 12.3 percent did. After 8 hours, the prevalence of delirium dropped to 9.2%, which means that 90.8% of patients exhibited no signs of delirium. It appears that the frequency of postoperative delirium has been declining.

Table 4.3 Postoperative Delirium Status

Time Interval After Surgery	Delirium Present	Frequency (n=163)	Percentage (%)
2 hours	Yes	30	18.4
	No	133	81.6
4 hours	Yes	25	15.3
	No	138	84.7
6 hours	Yes	20	12.3
	No	143	87.7
8 hours	Yes	15	9.2
	No	148	90.8

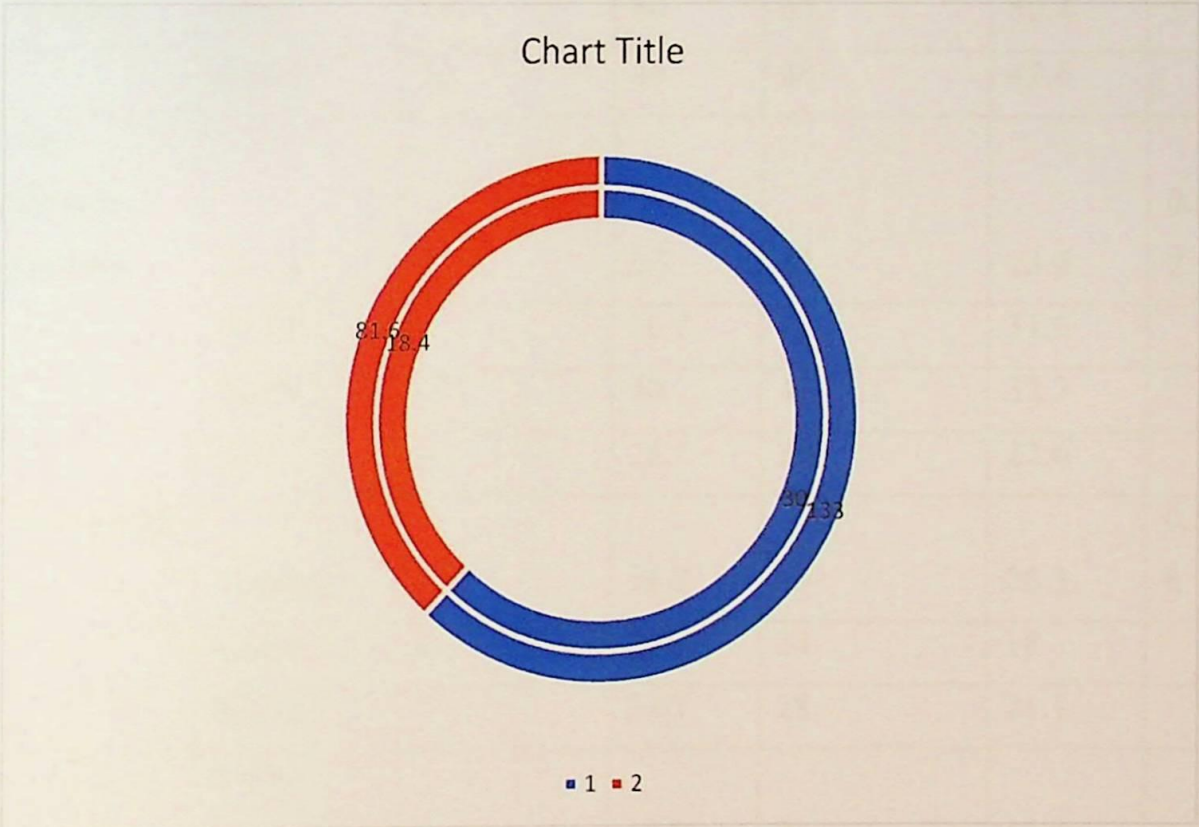


Figure 4.5 Postoperative Delirium Status

When comparing demographic and clinical factors between those with delirium and those without, the findings are statistically significant. Statistical analysis revealed a correlation between BMI and delirium ($p = 0.04$); patients who were obese were more likely to experience delirium (33.3% vs. 53.3%). The prevalence of increased HbA1c levels ($>7.5\%$) was 40% in the delirium group and 23.3% in the non-delirium group ($p = 0.03$). Over an hour-long procedure was associated with a 60% higher risk of

delirium compared to the 1–2-hour group ($p = 0.02$). A significantly higher percentage of delirious patients (43.3%) compared to the control group (28.0%) had fasting blood glucose levels ranging from 130 to 180 mg/dl ($p = 0.01$). Postoperative delirium seemed to be more common in some groups, but other demographics including age, education level, gender, and the outcomes of kidney and liver tests did not differ significantly between the groups.

Table 4.4 comparison of demographic characteristic among delirium status

Variable	Category	Delirium Present (n=30)	Percent age (%)	Delirium Absent (n=133)	Percent age (%)	p-value
Gender	Male	18	60	67	50.4	0.35
	Female	12	40	66	49.6	
Age Group (years)	30-39	2	6.7	18	13.5	0.42
	40-49	8	26.7	42	31.6	
	50-59	12	40	43	32.3	
	60+	8	26.7	30	22.6	
Occupation	Teacher	5	16.7	35	26.3	0.58
	Nurse	6	20	24	18	
	Retired	7	23.3	28	21.1	
	Office Worker	4	13.3	21	15.8	
	Other	8	26.7	25	18.8	
Education Level	High School	15	50	55	41.4	0.55
	Diploma	10	33.3	40	30.1	
	Bachelor's Degree	5	16.7	38	28.6	
Type of Diabetes	Type I	8	26.7	52	39.1	0.24

	Type II	20	66.7	75	56.4	
	Gestational	2	6.7	6	4.5	
BMI Category	Normal (18.5 - 24.9)	4	13.3	36	27.1	0.04*
	Overweight (25 - 29.9)	16	53.3	54	40.6	
	Obese (30 and above)	10	33.3	43	32.3	
Duration of Diabetes	< 5 years	6	20	34	25.6	0.72
	5-10 years	12	40	48	36.1	
	> 10 years	12	40	51	38.3	
HbA1c Level	< 6.5%	5	16.7	45	33.8	0.03*
	6.5% - 7.5%	13	43.3	57	42.9	
	> 7.5%	12	40	31	23.3	
Operation Duration	< 1 hour	6	20	54	40.6	0.02*
	1-2 hours	18	60	62	46.6	
	> 2 hours	6	20	17	12.8	
Fasting Blood Sugar	< 130 mg/dl	10	33.3	80	60.2	0.01*
	130-180 mg/dl	13	43.3	37	27.8	
	> 180 mg/dl	7	23.3	16	12	
Renal Function Test	Normal	18	60	102	76.7	0.09

	Mildly Abnormal	8	26.7	22	16.5	
	Moderately Abnormal	4	13.3	9	6.8	
Liver Function Test	Normal	22	73.3	108	81.2	0.3 6
	Mildly Abnormal	6	20	19	14.3	
	Severely Abnormal	2	6.7	6	4.5	

The incidence of postoperative nausea and vomiting (PONV) or its absence was found to be significantly correlated with a number of variables. Type II diabetic patients had a significantly higher incidence of PONV (71.4% vs. 26.9% in the non-PONV group, $p = 0.002$), as did individuals with higher body mass index (BMI) categories. There was a link between HbA1c levels and PONV, and a lower HbA1c level ($<6.5\%$) was more prevalent in the group that did not experience postoperative nausea and vomiting (PONV) (37.6%, $p = 0.02$). The percentage of operations lasting less than an hour was lower in the PONV group (14.3 percent vs. 37.6 percent, $p = 0.01$). Patients whose fasting blood glucose levels were high (130-180 mg/dl, $p = 0.003$) had a 50% increased incidence of postoperative nausea and vomiting (PONV). In addition, the frequency of abnormal liver function tests was significantly higher in the PONV group (28.5% vs. 14%, $p = 0.04$). There were no statistically significant differences in the occurrence of PONV by age group, renal function, education level, or gender.

Table 4.5 comparison of demographic characteristics among Post-Operative Nausea and Vomiting

Variable	Category	PONV Present (n=70)	Percent age (%)	PONV Absent (n=93)	Percent age (%)	p-value
Gender	Male	40	57.1	45	48.4	0.2 8
	Female	30	42.9	48	51.6	

Age Group (years)	30-39	8	11.4	12	12.9	0.7 3
	40-49	20	28.6	30	32.3	
	50-59	30	42.9	25	26.9	
	60+	12	17.1	26	28	
Occupatio n	Teacher	12	17.1	28	30.1	0.1 4
	Nurse	15	21.4	15	16.1	
	Retired	18	25.7	17	18.3	
	Office Worker	10	14.3	15	16.1	
	Other	15	21.4	18	19.4	
Education Level	High School	30	42.9	40	43	0.9 9
	Diploma	20	28.6	30	32.3	
	Bachelor's Degree	20	28.6	23	24.7	
Type of Diabetes	Type I	15	21.4	45	48.4	0.0 02*
	Type II	50	71.4	46	49.5	
	Gestational	5	7.1	2	2.2	
BMI Category	Normal (18.5 - 24.9)	12	17.1	28	30.1	0.0 1*
	Overweight (25 - 29.9)	30	42.9	40	43	
	Obese (30 and above)	28	40	25	26.9	
Duration of Diabetes	< 5 years	15	21.4	25	26.9	0.4 1
	5-10 years	28	40	32	34.4	
	> 10 years	27	38.6	36	38.7	
HbA1c Level	< 6.5%	15	21.4	35	37.6	0.0 2*

	6.5% - 7.5%	35	50	35	37.6	
	> 7.5%	20	28.6	23	24.7	
Operation Duration						0.0
	< 1 hour	10	14.3	35	37.6	1*
	1-2 hours	45	64.3	40	43	
	> 2 hours	15	21.4	18	19.4	
Fasting Blood Sugar						0.0
	< 130 mg/dl	20	28.6	50	53.8	03*
	130-180 mg/dl	35	50	30	32.3	
	> 180 mg/dl	15	21.4	13	14	
Renal Function Test						0.3
	Normal	48	68.6	70	75.3	6
	Mildly Abnormal	15	21.4	18	19.4	
	Moderately Abnormal	7	10	5	5.4	
Liver Function Test						0.0
	Normal	50	71.4	80	86	4*
	Mildly Abnormal	15	21.4	10	10.8	
	Severely Abnormal	5	7.1	3	3.2	

Using logistic regression analysis, we were able to identify a number of significant risk factors for postoperative nausea and vomiting (PONV). Postoperative nausea and vomiting (PONV) were more common in patients with Type II diabetes compared to Type I diabetes (OR = 2.25, 95% CI: 1.27-3.97, $p = 0.005$). The odds ratio (OR) for postoperative nausea and vomiting (PONV) was 1.75 (95% CI: 1.03-2.97, $p = 0.04$), which was higher in obese individuals than in normal-weight patients. With an odds

ratio (OR) of 1.55 (95% CI: 1.01-2.37, $p = 0.04$), postoperative nausea and vomiting (PONV) was substantially linked to over 7.5% HR. In addition, the odds ratio (OR) for postoperative nausea and vomiting (PONV) was 2.15 (95% CI: 1.01-4.56, $p = 0.05$) for operations lasting 1-2 hours and 1.8 (95% CI: 1.06-3.06, $p = 0.03$) for operations lasting more than 2 hours. Patients with fasting blood sugar levels greater than 180 mg/dl had a substantially increased odds ratio (OR) for postoperative nausea and vomiting (PONV) 2.1 (95% CI: 1.12-3.92, $p = 0.02$). None of the other factors tested, including gender, age, renal or liver function tests, and PONV, were shown to have statistically significant correlations according to this model.

Table 6 Regression analysis among respondents/patients for postoperative nausea and vomiting

Variable	Category	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Gender	Male (ref)	1	-	-
	Female	1.35	0.85 – 2.14	0.2
Age Group (years)	30-39 (ref)	1	-	-
	40-49	1.22	0.68 – 2.19	0.5
	50-59	1.65	0.90 – 3.05	0.1
	60+	1.1	0.55 – 2.21	0.78
Occupation	Teacher (ref)	1	-	-
	Nurse	1.45	0.75 – 2.79	0.27
	Retired	1.85	1.01 – 3.39	0.04*
	Office Worker	1.2	0.60 – 2.41	0.62
	Other	1.1	0.59 – 2.07	0.78
Education Level	High School (ref)	1	-	-
	Diploma	1.18	0.65 – 2.12	0.58
	Bachelor's Degree	1.08	0.55 – 2.13	0.81
Type of Diabetes	Type I (ref)	1	-	-
	Type II	2.25	1.27 – 3.97	0.005*
	Gestational	1.05	0.38 – 2.91	0.92
BMI	Normal (ref)	1	-	-

	Overweight	1.42	0.85 – 2.37	0.19
	Obese	1.75	1.03 – 2.97	0.04*
Duration of Diabetes	< 5 years (ref)	1	-	-
	5-10 years	1.23	0.72 – 2.11	0.45
	> 10 years	1.33	0.77 – 2.28	0.3
HbA1c Level	< 6.5% (ref)	1	-	-
	6.5% - 7.5%	1.32	0.81 – 2.15	0.27
	> 7.5%	1.55	1.01 – 2.37	0.04*
Operation Duration	< 1 hour (ref)	1	-	-
	1-2 hours	1.8	1.06 – 3.06	0.03*
	> 2 hours	2.15	1.01 – 4.56	0.05*
Fasting Blood Sugar	< 130 mg/dl (ref)	1	-	-
	130-180 mg/dl	1.55	0.95 – 2.53	0.07
	> 180 mg/dl	2.1	1.12 – 3.92	0.02*
Renal Function Test	Normal (ref)	1	-	-
	Mildly Abnormal	1.3	0.72 – 2.36	0.38
	Moderately Abnormal	1.85	0.89 – 3.84	0.1
Liver Function Test	Normal (ref)	1	-	-
	Mildly Abnormal	1.45	0.82 – 2.57	0.2
	Severely Abnormal	2.25	0.98 – 5.15	0.06

CHAPTER 5

DISCUSSION

The effects of ketamine administration during laparoscopic cholecystectomy were examined in this study. Our results show that esketamine can decrease stress and inflammatory reactions. Additionally, less elicitation of excitatory sympathetic responses contributed to the avoidance of intraoperative hypotension. Additionally, esketamine improved cognitive scores the day after surgery, decreased opioid intake, and accelerated recovery from anaesthesia.

The less invasive nature of LC technology makes it an obvious choice for therapeutic purposes. A carbon dioxide pneumoperitoneum, when established during surgery, negatively impacts postoperative breathing, blood flow, and cognitive function. An increase in intra-abdominal pressure, known as pneumoperitoneum, causes the diaphragm to rise, which in turn causes an increase in intrapulmonary pressure. Lung compliance is changed because of this shift (19). Hypoxia, ischemia, and an overabundance of reactive oxygen species (ROS) are linked symptoms of reduced venous flow to the central nervous system (CNS) caused by compression of the abdomen arteries. One major cause of postoperative cognitive dysfunction (POCD) is inflammation in the central nervous system. Angiotensin II and other peripheral inflammatory mediators are highly correlated with CNS inflammation (20,21). When the SANS is activated during surgery, the pneumoperitoneum increases the signal strength, which in turn increases the peripheral release of norepinephrine and inflammatory cytokines. Carbon dioxide's partial pressure is rapidly increasing, exacerbating the problem. The interaction between microglial cells and hypercapnia leads to an overproduction of the cytokine IL-1 β , which in turn triggers the release of more inflammatory mediators. Cognitive impairments associated with this inflammatory cascade include problems with hippocampus-dependent memory (22). Careful management of intraoperative analgesia and inotropic relaxation is required for LC to be effective, as is the real-time adjustment of circulation and breathing to compensate for physiological changes produced by CO₂ pneumoperitoneum. In this way, hemodynamic stability and a rapid postoperative recovery are guaranteed. The patients receiving ketamine usually have low levels of epinephrine and endorphine, so patients usually stay hemodynamically stable during surgery (23,24). The results

corroborate earlier research demonstrating that esketamine's effects are dose-dependent; that it indirectly enhances cardiovascular function, resulting in elevated blood pressure, heart rate, and cardiac output; and that it has minimal influence on peripheral vasculature, indicating that it can be safely used during perioperative periods.

Patients show shorter periods of postoperative arousal and reduced use of intraoperative remifentanyl, propofol, and 24-hour sufentanyl. Consistent with previous studies, these findings demonstrate that the main cause of fast arousal is the redistribution and metabolism of the sedative medicine. One of the ways that esketamine is transformed into nor-esketamine is by the action of liver microsomal enzymes. Pharmacologically, nor-esketamine is active, and its anesthetic potency is around a fifth to a third of esketamine's (25,26). The analgesic effects of esketamine continue long after patients awaken from anesthesia due to its extended elimination half-life. Furthermore, esketamine inhibits hypersensitization-inducing alterations in the dorsal horn of the spinal cord by blocking the glutamate NMDA receptor. Esketamine doesn't just dull pain; it also decreases opioid consumption, boosts analgesia following surgical incisions, and eases opioid-induced nociceptive hyperalgesia via its actions on peripheral NMDA receptors. One possible mechanism by which esketamine reduces pain is via activating microglia potassium channels with calcium ions. Low doses of esketamine can make the patient's awakening more bearable by reducing the intensity of the choking reflex during recovery from general anesthesia and by making the waking process easier with fewer side effects. Our group's opioid-sparing effects are in line with these results (27,28).

Postoperative nausea and vomiting (PONV) is higher in the elderly due to age-related changes in organ function and poorer resistance to surgical trauma. Furthermore, from 18.4% at 2 hours post-surgery to 9.2% at 8 hours, the study found that the prevalence of delirium decreased significantly over time. The frequency of PONV at various time intervals was also examined. Both obesity and type II diabetes were associated with a substantially higher risk of delirium, as seen by the large p-values for these conditions. Additionally, delirium was more common in patients with high fasting blood sugar levels (>180 mg/dl). Type II diabetes, obesity, and longer surgical procedures were associated with an increased risk of postoperative nausea and vomiting (PONV). Opioid use following surgery was initially restricted after it was found to be a major factor to postoperative nausea and vomiting (PONV). Under anaesthesia, S-ketamine

also helped keep hemodynamic stability (31,32). Insufficient blood flow to the brainstem and vestibular system after surgery can sometimes cause the release of substances such as serotonin, histamine, and cytokines (33,34). By binding to serotonin and histamine receptors, these compounds may trigger the chemoreceptor regions, leading to the gastrointestinal side effects of nausea and vomiting. Based on previous research, opioid-free anesthesia is a great option for patients who are at high risk for postoperative nausea and vomiting (PONV) since it lessens the severity of these symptoms.

CONCLUSION

The study found that the prevalence of delirium decreased significantly over time from 18.4% at 2 hours post-surgery to 9.2% at 8 hours. The causes of postoperative delirium were found being overweight, having high HbA1c levels, and having a lengthy operation. Both obesity and type II diabetes were associated with a substantially higher risk of delirium, as seen by the large p-values for these conditions. Additionally, delirium was more common in patients with high fasting blood sugar levels (>180 mg/dL). Type II diabetes, obesity, and longer surgical procedures were associated with an increased risk of postoperative nausea and vomiting (PONV). These findings highlight the need of managing preoperative complications, such as diabetes and obesity, in order to reduce the likelihood of complications like delirium and postoperative nausea and vomiting (PONV).

Limitations

Limitations to this study includes:

- The relatively small sample size of 163 participants limits the generalizability of the findings
- Conducting this study in a single setup restricts the ability to generalize results to other healthcare settings.

Recommendations

Based on the study findings, we suggest the following recommendations:

- Enhanced preoperative assessment of the patient could minimize the chances of postoperative nausea and vomiting and POCD.
- Standardized Protocols should be in practice in order to minimize the chances of PONV and POCD. This can be achieved through trainings and education.
- For future research we recommend Multi-Center Research studies, which could help further to identify and explore means to reduce potential complications of anesthesia.

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APPENDICES

APPENDIX-1

INFORMED CONSENT

You are invited to participate in a research study titled "*The Impact of Ketamine on Postoperative Nausea, Vomiting, and Cognitive Dysfunction in Diabetic Patients Undergoing Laparoscopic Cholecystectomy.*" This study aims to evaluate the effects of ketamine on postoperative nausea, vomiting (PONV), and cognitive dysfunction in diabetic patients. If you agree to participate, you will receive a carefully calculated dose of ketamine or a placebo during your surgery. Your health will be closely monitored before, during, and after surgery, with specific evaluations of nausea, vomiting, and cognitive function at various intervals. Participation involves no additional procedures beyond the standard care for your surgery, apart from the administration of ketamine or placebo.

The study poses minimal risks, including mild, short-term side effects of ketamine such as dizziness or mild hallucinations. However, all necessary precautions will be taken to ensure your safety. While there are no direct financial benefits, you may experience reduced PONV, and your participation will contribute to advancing medical knowledge and improving care for future patients. Your personal information will remain strictly confidential, and all data collected will be anonymized.

Participation is entirely voluntary, and you have the right to withdraw from the study at any time without affecting your medical care. If you have any questions or concerns, you are encouraged to contact the principal investigator. By signing the consent form, you acknowledge that you understand the study's purpose, procedures, risks, and benefits and that you voluntarily agree to participate.

Thank you for considering participation in this important research.

Consent Statement:

By signing below, you confirm that:

- You have read and understood the purpose, procedures, risks, and benefits of this study.
- You have had an opportunity to ask questions and have them answered to your satisfaction.
- You voluntarily agree to participate in this study.

Participant's Name: _____

Participant's Signature: _____

Date: _____

Investigator's Name: _____

Investigator's Signature: _____

Date: _____

APPENDIX-2

Ethical Approval



OFFICE OF THE DEAN-FAHS

SUPERIOR UNIVERSITY

Ref.: IRB /FAHS/Allied-HS/10/24/MS/RS-3480

Date: 29th October 2024

Name: Amna Saleem (MS Allied Health Sciences)

Registration: SU91-MSAHW-S23-025

Subject: Ethical Approval Letter

The Research Ethical Committee convened on Dated: 17th October, 2024 to discuss your protocol titled "**The impact of ketamine on postoperative nausea, vomiting, and cognitive dysfunction in diabetic patients undergoing laparoscopic cholecystectomy**"

No further corrections and recommendations were suggested. The above-mentioned protocol has been approved after considering various research issues including ethical concerns with condition that the researcher will submit completion report at the end of his/her research.

Prof. Dr. Muhammad Naveed Babur
Dean/Convener REC
Faculty of Allied Health Sciences
Superior University, Lahore

APPENDIX-3

QUESTIONNAIRE

Part 1: Demographic Information

- Age: _____ years

- Gender:

- Male
- Female

Occupation: _____

Education Level: _____

Medical History

- Height: _____ cm

- Weight: _____ kg

- Body Mass Index (BMI): _____ kg/m²

Part 2: Clinical and Laboratory Reports

1. Diabetes Information

- Type of Diabetes:

- Type I
- Type II
- Gestational

- Duration of Diabetes: _____ years

- Latest HbA1c Level: _____ % (if available)

- Operation Duration _____
- Intraoperative Blood Loss _____

2. Laboratory Reports

- Fasting Blood Sugar FBS _____

Renal Function Test RFT _____

LFT _____

Part 3: Postoperative Assessment

Postoperative Nausea and Vomiting (PONV)

Please circle the most appropriate response for each question:

1. **Have you experienced any nausea since your surgery?**
 - ☐ No nausea
 - ☐ Mild nausea
 - ☐ Moderate nausea
 - ☐ Severe nausea
2. **Have you experienced any vomiting since your surgery?**
 - ☐ No vomiting
 - ☐ Vomited once
 - ☐ Vomited multiple times
3. **If you experienced nausea, how would you rate its severity on a scale of 0 to 10 (0 being no nausea and 10 being the worst possible nausea)?**
 - ☐ 0 1 2 3 4 5 6 7 8 9 10
4. **If you experienced vomiting, how many times did you vomit?**
 - ☐ 0 times
 - ☐ 1-2 times
 - ☐ 3-4 times
 - ☐ More than 4 times
5. **At what times after the surgery did you experience nausea and/or vomiting? (Check all that apply)**
 - ☐ 0-2 hours
 - ☐ 2-6 hours
 - ☐ 6-12 hours
 - ☐ 12-24 hours
6. **Did you take any medication to relieve nausea or vomiting?**
 - ☐ Yes
 - ☐ No

- If yes, please specify: _____
- 7. **How effective was the medication in relieving your nausea/vomiting?**
 - Not effective
 - Somewhat effective
 - Effective
 - Very effective
- 8. **Have you experienced any other symptoms or side effects since your surgery? (Check all that apply)**
 - Dizziness
 - Headache
 - Fatigue
 - Other (please specify): _____
- 9. **On a scale of 0 to 10, how would you rate your overall comfort level since the surgery? (0 being the least comfortable and 10 being the most comfortable)**
 - 0 1 2 3 4 5 6 7 8 9 10

Part 4: Richmond Agitation-Sedation Scale (RASS) and CAM-ICU Assessments

The RASS scores range from +4 (combative) to -5 (unarousable). Healthcare providers assess the patient's level of alertness and response to stimuli. The scale is applied as follows:

- +4: Combative – Overtly combative or violent; immediate danger to staff.
- +3: Very agitated – Pulls or removes tube(s) or catheter(s); aggressive.
- +2: Agitated – Frequent non-purposeful movement or fights ventilator.
- +1: Restless – Anxious or apprehensive but movements are not aggressive or vigorous.
- 0: Alert and calm.
- -1: Drowsy – Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice.
- -2: Light sedation – Briefly (less than 10 seconds) awakens with eye contact to voice.

- -3: Moderate sedation – Any movement (but no eye contact) to voice.
- -4: Deep sedation – No response to voice, but any movement to physical stimulation.
- -5: Unarousable – No response to voice or physical stimulation.

1. Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)

The CAM-ICU involves a structured assessment to identify the presence of delirium based on four features:

1. **Acute onset of mental status changes or a fluctuating course:** Assessed by changes in the patient's baseline mental status.
2. **Inattention:** Determined by the patient's ability to focus attention, often tested through a series of tasks (e.g., the "SAVEAHAART" test, where the patient is asked to squeeze the examiner's hand when they hear the letter "A").
3. **Disorganized thinking:** Assessed by asking the patient simple questions or giving commands (e.g., asking them to hold up two fingers or asking if a stone can float on water).
4. **Altered level of consciousness:** Evaluated using the RASS, where anything other than a score of zero indicates an altered level of consciousness.

The diagnosis of delirium is confirmed if the patient exhibits features 1 and 2, plus either feature 3 or 4.

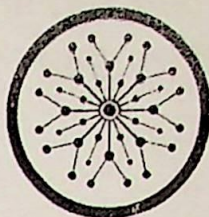
1. RASS Assessments

- Please indicate your RASS score at each of the following intervals post-surgery:
 - 2 hours: _____ (score)
 - 4 hours: _____ (score)
 - 6 hours: _____ (score)
 - 8 hours: _____ (score)

2. CAM-ICU Assessments

- Please complete the CAM-ICU assessment at the same intervals post-surgery:
 - 2 hours: Delirium Present / Absent
 - 4 hours: Delirium Present / Absent

- 6 hours: Delirium Present / Absent
- 8 hours: Delirium Present / Absent



PLAGIARISM CERTIFICATE

For MPhil and PhD

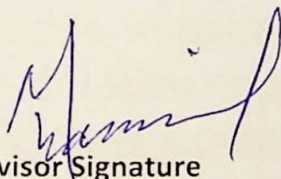
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Student Name: Amna Saleem

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